REMARKS

Claims 60, 62, and 65-91 are pending.

Priority

The Office Action stated that the claims are not entitled to the priority date of U.S. Patent Application Serial No. 09/204,254 (now U.S. Patent No. 6,369,039; hereinafter "the '039 patent"). The Office Action provided two reasons for this conclusion:

(1) The '039 patent does not contain a written description of the subgenus of angiogenic agents supposedly set forth in the claims. See the Office Action, paragraph bridging pages 2-3:

> However, the list set forth in the new claims does not include all of the products listed in the specification [of the ''039 patent] that are considered angiogenic agents (e.g., hif-1). The specification [of the ''039 patent] does not disclose the subgenus set [sic, forth?] in the new claims and claims dependent therefrom. Thus, nothing in the specification [of the '039 patent] would lead one to the particular combination set forth in the amended and claims dependent therefrom and new claims [sic].

The Applicant wishes to point out that the present claims do not contain a list of angiogenic agents that is a subgenus of any lists disclosed in the '039 patent. The Applicant believes that the present claims are as shown in the Appendix to this paper. Certain of the present dependent claims recite particular angiogenic agents but no lists of angiogenic agents appear in the present claims. Accordingly, it does not seem that the Office Action's comments are applicable to the present claims.

(2) All the present claims recite a combination of an angiogenic agent and a polynucleotide encoding an angiogenic agent. In its discussion of the dependent claims, the Office Action argued that there is no disclosure in the '039 patent of the use of both an

angiogenic agent and a polynucleotide encoding an angiogenic agent. Instead, according to the Office Action, the '039 patent only discloses the use of either an angiogenic agent or a polynucleotide encoding an angiogenic agent. See, e.g., the Office Action, page 3, second paragraph from bottom:

> [W]hile it is acknowledged that acidic or basic fibroblast growth factor or DNA encoding acidic or basic fibroblast growth factor is listed in col. 5, line 66 [of the '039 patent], the limitation is directed to either acidic or basic fibroblast growth factor or DNA encoding acidic or basic fibroblast growth factor. The limitation does not embrace using an acidic or basic fibroblast growth factor and DNA encoding either factor. There is nothing in the specification of '039 to lead the skilled artisan to using both in the medical device.

The Applicant respectfully disagrees. The combination of an angiogenic agent and a polynucleotide encoding an angiogenic agent is disclosed in the paragraph at col. 5, l. 49 to col. 6, l. 22 of the '039 patent. In this passage, the '039 patent first makes clear that the polymeric coating of the devices described therein can include polynucleotides encoding therapeutic agents ("Polynucleotide sequences useful in practice of the invention include DNA or RNA sequences having a therapeutic effect after being taken up by a cell;" col. 5, ll. 49-51). The '039 patent then states that, **in addition to** the polynucleotides, the polymeric coating may contain polypeptides and proteins ("In addition, the polypeptides or proteins that can be incorporated into the polymeric coating ... ;" col. 5, ll. 62-64). This is followed by a list of suitable therapeutic agents, including the angiogenic agents that are recited in the present claims.

The combination of an angiogenic agent and a polynucleotide encoding an angiogenic agent is also disclosed in the paragraph at col. 4, l. 64 to col. 5, l. 48. This paragraph teaches that polynucleotides (col. 4, l. 67, to col. 5, l. 4) and angiogenic agents (col. 5, ll. 15-16) can be in the polymeric coating. It is then stated that combinations of polynucleotides and

angiogenic agents can be in the coating ("and combinations thereof;" col. 5, l. 44). That the polynucleotides may encode angiogenic agents is taught at col. 5, ll. 62-65.

The present claims are therefore entitled to the priority date of U.S. Patent Application Serial No. 09/204,254 (now U.S. Patent No. 6,369,039).

Accordingly, it is respectfully requested that the denial of priority be reconsidered.

The rejection under 35 U.S.C. §112

The claims were rejected for failure to comply with the written description requirement because the present specification supposedly does not disclose the use of both an angiogenic agent and a polynucleotide encoding an angiogenic agent. See the Office Action, page 6, last paragraph:

> [T]he specification discloses that either the first or the second polynucleotide or both encode the angiogenic agents. There is no disclosure in the specification of an angiogenic agent and a polynucleotide encoding an angiogenic agent.

The Applicant respectfully traverses this rejection. The present claims have written description support in the present application. In particular, the present application discloses the use of an angiogenic agent and a polynucleotide encoding an angiogenic agent. This can be readily seen by examining the following table, which demonstrates that the language of claim 60 closely tracks the language found in the Summary of the Invention of the present application (page 5, lines 3-11). This comparison demonstrates the presence of the

combination of an angiogenic agent and a polynucleotide encoding an angiogenic agent in both claim 60 and the Summary of the Invention.

Claim 60	Summary of the Invention Page 5, lines 3-11
A medical device comprising:	... a medical device having
a biocompatible structure comprising a polymeric coating that coats at least a portion of said structure, said polymeric coating comprising:	a biocompatible structure carrying a genetic material. The biocompatible structure comprises a biocompatible polymeric coating that coats at least a portion of the structure and carries a genetic material. The genetic material comprises:
(A) a therapeutic agent, wherein said therapeutic agent is an angiogenic agent, and	(a) a second[1] therapeutic agent comprising at least one of (i) a second polynucleotide carried by a carrier; (ii) a protein; (iii) **a non-genetic therapeutic agent**, or (iv) cells [emphasis added]
(B) a vector containing a polynucleotide that establishes a gene expression sufficient to produce a therapeutically sufficient amount of one or more products encoded by said polynucleotide, wherein said polynucleotide encodes a polypeptide or protein, wherein said polypeptide or protein is an angiogenic agent.	(b) a first therapeutic agent comprising a vector containing a first polynucleotide that establishes a gene expression sufficient to produce a therapeutically sufficient amount of one or more products encoded by said first polynucleotide

The primary difference between claim 60 and the disclosure at page 5, lines 3-11 is that claim 60 limits the first therapeutic agent at page 5, line 6 to a polynucleotide encoding an angiogenic agent and claim 60 limits the second therapeutic agent (i.e., the non-genetic therapeutic agent at page 5, line 10) to an angiogenic agent. Support for these limitations

[1] For ease of comparison to claim 60, (a) and (b) from the disclosure at page 5, lines 3-11 have been transposed.

with respect to angiogenic agents is found in those portions of the present application that teach that both the therapeutic agents may be angiogenic agents. See, e.g., page 18, line 1.

See also original claim 33, which states that "said first therapeutic agent, said second therapeutic agent, **or both**" [emphasis added] can be angiogenic agents. Original claim 33 depends from original claim 26, which, in one of its embodiments, is directed to the combination of a polynucleotide and a non-genetic therapeutic agent. Thus, original claim 33 teaches that the Applicant contemplated the combination of a polynucleotide and a non-genetic therapeutic agent where both the polynucleotide encodes an angiogenic agent and the non-genetic therapeutic agent is an angiogenic agent.

One or ordinary skill in the art is again directed to this combination at page 22, line 21 to page 23, line 6, where a preferred embodiment of the invention is disclosed as:

> A preferred embodiment of this invention is to provide treatment of vascular thrombosis and angioplasty restenosis, particularly coronary vascular thrombosis, and angioplasty restenosis, thereby to decrease incidence of vessel rethrombosis and restenosis, unstable angina, myocardial infarction and sudden death. The medical device and method of this invention can be used to treat patients having severe complications resulting from thrombus. Specific examples include patients with acute myocardial infarction (AMI) and patients that have failed PTCA (percutaneous transluminal coronary angioplasty) and have abrupt thrombotic closure of the targeted artery.

From this passage, one of ordinary skill in the art would recognize that one aspect of the invention is designed to increase blood flow and thereby oxygen delivery to tissues, particularly to tissues sensitive to disruptions in cardiovascular perfusion. One of ordinary skill in the art would recognize that this can be accomplished through a local increase of blood flow by the development and expansion of blood vessels in an area of potential stenosis or thrombotic blockage, i.e., by angiogenesis. Thus, this passage directs one of ordinary skill in the art to the choice of "angiogenic agents" as the therapeutic agents of the invention.

Furthermore, in Example 7 on pages 28-29, the specification discloses an embodiment in which both therapeutic agents are "angiogenic agents." This example discloses a medical device comprising polynucleotides encoding VEGF protein and FAS Ligand protein.

The specification indicates that VEGF protein is a "promoter of endothelialization" (Example 7, page 29, line 3), i.e., an angiogenic agent. Moreover, it is well known in the art that VEGF protein is known to play a critical and central role in angiogenesis. FAS Ligand is also well-known to promote angiogenesis.

Thus, Example 7 clearly directs the skilled person to the concept of practicing the invention wherein **both** therapeutic agents are angiogenic agents. Although Example 7 describes the use of two genetic therapeutic agents rather than the presently claimed combination of a genetic therapeutic agent and a non-genetic therapeutic agent, the concept of using both a genetic therapeutic agent and a non-genetic therapeutic agent is clearly described elsewhere (see discussion above) and would have been understood as being suitable for combination with the concept of Example 7 that both therapeutic agents can be angiogenic agents.

Other portions of the present application also provide written description support for the recited combination of an angiogenic agent and a polynucleotide encoding an angiogenic agent.

The combination of a therapeutic agent comprising genetic material, e.g., a polynucleotide, with a non-genetic therapeutic agent is clearly disclosed at page 17, lines 6-8:

> The first therapeutic agent of this invention comprises genetic materials whereas the second therapeutic agent of the invention may comprise either genetic or non-genetic materials.

The reference to the "first therapeutic agent" in this passage would be understood in light of prior disclosures in the specification which teach that the "first therapeutic agent" is preferably a polynucleotide. See, e.g., page 5, lines 6-7 ("a first therapeutic agent comprising ... a first polynucleotide ..."); page 6, line 9 ("a first therapeutic agent comprising ... a first polynucleotide ..."). Thus, the passage at page 17, lines 6-8 quoted above would be understood as teaching the combination of a first therapeutic agent that is a polynucleotide with a non-genetic therapeutic agent.

In the second paragraph after the above disclosure at page 17, lines 6-8 of the combination of a first therapeutic agent that is a polynucleotide with a non-genetic therapeutic agent, there is a disclosure that both therapeutic agents can be angiogenic agents (page 18, line 1). The disclosures at page 17, lines 6-8 and page 18, line 1 would be reinforced by original claim 33; page 22, line 21 to page 23, line 6; and Example 7, all of which, as explained above, teach that the Applicant contemplated the combination of a polynucleotide and a non-genetic therapeutic agent where the polynucleotide encodes an angiogenic agent and the non-genetic therapeutic agent is an angiogenic agent.

The Office Action stated, at page 6, 4th paragraph, that the "instant specification does not disclose the subgenus set forth in the new claims."

As explained above, the present claims do not contain a list of angiogenic agents that is a subgenus of any lists disclosed in the present application. Accordingly, it does not seem that the Office Action's comments with respect to "the subgenus set forth in the new claims" are applicable to the present claims.

In view of the above, it is respectfully requested that this rejection be withdrawn.

The rejections under 35 U.S.C. §103(a)

Claims 60, 62, 65, 67, 68, 69, 71, 72, 73, 75, 77-80, 82-84, 86, 87, 88, 90, and 91 were rejected as being obvious over U.S. Patent No. 5,879,713 (Roth) taken with U.S. Patent No. 5,869,037 (Crystal).

The Applicant respectfully traverses this rejection. The present claims contain the limitation of a polymeric **coating** comprising both an angiogenic agent and a polynucleotide encoding an angiogenic agent. Even if it were proper to combine Roth and Crystal, the combination of Roth and Crystal would not provide this limitation.

Roth does not disclose this limitation. Roth does not disclose any polymeric **coating** at all on a medical device. Instead, Roth discloses that polymeric material comprising desired substances should be loaded **in** medical devices (e.g., a balloon catheter) and then used to form a coating **on the surface of the tissue**. See col. 11, ll. 43-53:

> Local administration of a polymeric material can be performed by loading the composition **in** a balloon catheter, and then applying the composition directly to the inside of a tissue lumen within a zone occluded by the catheter balloons. The tissue surface may be an internal or external surface, and can include the interior of a tissue lumen or hollow space whether naturally occurring or occurring as a result of surgery, percutaneous techniques, trauma or disease. The polymeric material can then be reconfigured to form **a coating or "paving" layer in intimate and conforming contact with the surface**. [underscoring added]

The Applicant notes that the Office Action dated March 6, 2006 stated:

> In response to applicant's argument that Roth does not disclose a polymeric coating on a medical device, the argument is not found persuasive because Roth teaches loading the polymeric coating comprising the therapeutic agents onto a stent, which would indicate to the skilled artisan that the teaching of Roth would read on coating on a medical device.

The Office Action dated March 6, 2006 did not specify which portion of Roth was being referred to in the above quoted passage. The Applicant assumes it is the paragraph at col. 11, ll. 4-11,[2] which reads as follows:

> Preferred delivery methods are those which are minimally invasive or disruptive to the subject. These include administration of microparticles as well as percutaneous application to the interior of hollow organs or natural body cavities of a polymeric coating, film, gel, or stent. Suitable delivery devices for providing a polymer coating or layer on the surface of tissues are catheters, laparoscopes, and endoscopes, as defined in PCT/US94/94824 by Pathak et al.

There is no explicit disclosure that the polymeric coating referred to in this paragraph is present on the stent. Thus, the comment on the Office Action dated March 6, 2006 that this paragraph would suggest a "coating on a medical device" (i.e., a stent), is merely speculation. Accordingly, it should be disregarded.

Furthermore, the sentence in this paragraph containing the word "stent" reads: "These include administration of microparticles as well as percutaneous application to the interior of hollow organs or natural body cavities of a polymeric coating, film, gel, or stent." This sentence describes the application to hollow organs or body cavities of a polymeric coating, a film, a gel, **or** a stent ("... percutaneous application to the interior of hollow organs or natural body cavities of a polymeric coating, film, gel, **or** stent." [emphasis added]). The polymeric coating and the stent are disclosed as alternative substances that may be applied to the hollow organs or body cavities. There is no teaching that the polymeric coating is found on the surface of the stent.

The most natural interpretation of this passage is that it describes the common usage of a stent to prop open a hollow organ or a body cavity. This would allow the organ or cavity

[2] This is the only place in Roth where the word "stent" appears.

to remain open so that the "paving" layer described at col. 11, l. 52 could be placed on the interior of the hollow space thus formed ("The tissue surface may be an internal or external surface, and can include the interior of a tissue lumen or hollow space whether naturally occurring or occurring as a result of surgery, percutaneous techniques, trauma or disease. The polymeric material can then be reconfigured to form a coating or "paving" layer in intimate and conforming contact with the surface;" col. 11, ll. 47-53).

If instead Roth were disclosing the use of a polymeric coating on a stent, it would be expected that Roth would have taught how to apply the polymeric coating to the stent. But Roth did not.

Thus, not only is the interpretation in the Office Action dated March 6, 2006 speculation, it is implausible speculation since there is an alternative interpretation, not involving a stent with a polymeric coating, which is more in keeping with the rest of Roth's disclosure.

It should be further noted that the microparticles disclosed in Roth cannot be considered medical devices with polymeric coatings comprising an angiogenic agent and a polynucleotide encoding an angiogenic agent. Rather, Roth discloses that microparticles constitute a solid matrix in which biologically active substances are dispersed. See col. 9, ll. 24-26: "The matrix is preferably in the form of a microparticle such as a microsphere (where the biologically active molecules are dispersed throughout a solid polymeric matrix) ...").

Crystal also does not disclose a polymeric coating comprising an angiogenic agent and a polynucleotide encoding an angiogenic agent. Not only does Crystal not disclose this limitation, Crystal does not disclose a coating on a medical device at all. Crystal discloses that its vectors can be subjected to the usual techniques of pharmaceutical formulation (col.

11, ll. 14-28: "tablets, capsules, powders, granules, ointments, solutions, suppositories, injections, inhalants, and aerosols"). Crystal's working example involves injection through a syringe (col. 19, ll. 5-7: "The adenoviral vector was administered in a volume of 50 μl using a 0.5 ml syringe with a 30 gauge needle.").

In view of the lack of the disclosure of the limitation of a polymeric coating comprising an angiogenic agent and a polynucleotide encoding an angiogenic agent in both Roth and Crystal, it is respectfully requested that this rejection be withdrawn.

Claims 60, 62, 65, 66, 80, and 81 were rejected as being obvious over Roth taken with Crystal and further in view of U.S. Patent No. 5,851,521 (Branellec).

As discussed above, the combination of Roth and Crystal does not provide the limitation of a polymeric coating comprising an angiogenic agent and a polynucleotide encoding an angiogenic agent. Branellec was cited for its teaching of AAV vectors. Such teaching does not cure the defects of Roth and Crystal. Furthermore, Branellec does not disclose or suggest the limitation of a polymeric coating comprising an angiogenic agent and a polynucleotide encoding an angiogenic agent since Branellec does not disclose or suggest the combination of an angiogenic agent and a polynucleotide encoding an angiogenic agent.

Accordingly, it is respectfully requested that this rejection be withdrawn.

Claims 60, 62, 69, 70, 84 and 85 were rejected as being obvious over Roth taken with Crystal and further in view of U.S. Patent No. 5,833,651 (Donovan).

As discussed above, the combination of Roth and Crystal does not provide the limitation of a polymeric coating comprising an angiogenic agent and a polynucleotide encoding an angiogenic agent. Donovan was cited for its teaching of metallic stents. Such teaching does not cure the defects of Roth and Crystal. Furthermore, Donovan does not disclose or suggest the limitation of a polymeric coating comprising an angiogenic agent and a polynucleotide encoding an angiogenic agent since Donovan does not disclose or suggest the combination of an angiogenic agent and a polynucleotide encoding an angiogenic agent.

Accordingly, it is respectfully requested that this rejection be withdrawn.

Claims 60, 62, 74, 76, 89 were rejected as being obvious over Roth taken with Crystal and further in view of U.S. Patent No. 5,652,225 (Isner).

As discussed above, the combination of Roth and Crystal does not provide the limitation of a polymeric coating comprising an angiogenic agent and a polynucleotide encoding an angiogenic agent. Isner was cited for its teaching of VEGF, TGF-alpha, and TGF-beta. Such teaching does not cure the defects of Roth and Crystal. Furthermore, Isner does not disclose or suggest the limitation of a polymeric coating comprising an angiogenic agent and a polynucleotide encoding an angiogenic agent since Isner does not disclose or suggest the combination of an angiogenic agent and a polynucleotide encoding an angiogenic agent.

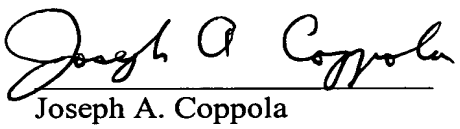
Accordingly, it is respectfully requested that this rejection be withdrawn.

The time for responding to the Office Action was set for November 15, 2006. Therefore, it is believed that this response is timely. If this is in error, please treat this response as containing a Petition for the Extension of Time under 37 C.F.R. § 1.136(a) for a period sufficient to permit the filing of this paper and charge any corresponding fees to Kenyon & Kenyon's Deposit Account No. 11-0600.

The Applicant hereby also makes a Conditional Petition for any relief available to correct any defect seen in connection with this filing, or any defect seen to be remaining in this application after this filing. The Commissioner is authorized to charge Kenyon & Kenyon's Deposit Account No. 11-0600 for any fees associated with such Conditional Petition.

Respectfully submitted,
KENYON & KENYON LLP

NOVEMBER 10, 2006
Date



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